This guidance was written prior to the February 27, 1997 implementation of FDA's Good Guidance Practices, GGP's. It does not create or confer rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. This guidance will be updated in the next revision to include the standard elements of GGP's.

AN
INTRODUCTION
TO

Medical Device Regulations

U.S. Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Devices and Radiological Health

AN INTRODUCTION TO MEDICAL DEVICE REGULATIONS

On May 28, 1976, the Food and Drug Administration (FDA) began implementing the Medical Device Amendments to the Federal Food, Drug & Cosmetic (FD&C) Act. These amendments give FDA specific authority to regulate "medical devices." Additional authority to regulate devices was provided in the Safe Medical Devices Act of 1990 (SMDA). The term "medical device" is defined as "... an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, that is:

- recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,

- intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease in man or other animals, or

- intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its principal intended purposes."

As this definition suggests, many different types of products are regulated as medical devices. Examples are wheelchairs, x-ray machines, pacemakers and glucose test kits.

CLASSIFICATION

If you engage in the manufacture, preparation, propagation, compounding, assembly, or processing of a device intended for human use that meets the earlier definition of a medical device, you are subject to regulations enforced by FDA. The level of regulation or control is governed by the "Class" in which your device is placed by the agency: Class I, II or III.

Classification recommendations by FDA are first published as proposals in the *Federal Register*. After receipt and consideration of comments, a final regulation classifying each device is published. As of the date of this pamphlet, all devices marketed before May 28, 1976 (preamendment devices) have been classified.

The three levels of control based on device class are:

Class I devices, those needing the lowest level of regulation, are subject to the "General Controls" requirements. These include establishment (manufacturing site) registration, device listing, Premarket Notification and Good Manufacturing Practices (GMP).

Class II devices are subject to "Special Controls" as well as "General Controls" requirements. Special Controls may include labeling, a mandatory performance standard, etc.

Class III devices cannot be marketed until they:

- have an approved Premarket Approval Application (PMA), *or*

- as a result of Premarket Notification [510(k)] submissions, have been found by FDA to be substantially equivalent to preamendment devices. If a PMA has been "called" for the type of preamendment device, however, a PMA must be submitted. (Premarket Notification is discussed in more detail later.)

Thus, the class of a device must be known to see what regulations apply to it. Note, however, that all devices, regardless of class, are subject to General Controls. Some Class I devices are exempt from the Premarket Notification and/or the Good Manufacturing Practices requirements. Exemptions are listed in the final classification regulation for the specific device.

GENERAL CONTROLS

Device firms must meet the following General Controls requirements:

- Register each manufacturing location (establishment).
- List marketed medical devices.
- Submit a "Premarket Notification" [510(k)] before marketing a device that is new to the firm or that has been significantly modified. If a contract manufacturer previously manufactured a device for a manufacturer, and the relationship has dissolved, the contract manufacturer must submit a 510(k) if it wishes to continue to manufacture and to distribute the device under its own labeling.
- Manufacture devices in accordance with the Good Manufacturing Practices (GMP) regulation.

These controls are explained below.

Establishment Registration

Unless exempt under 510(g) of the FD&C Act, the owner or operator of an establishment must register with FDA within 30 days after beginning any of these activities: manufacture, preparation, propagation, compounding, assembly, or processing of a device intended for human use. Activities requiring registration include repackaging, relabeling, distributing of imported or domestic devices, and specifications development.

Initial registration is made on the "Initial Registration Form" (FDA 2891). Thereafter, firms will receive an "Annual Registration Form" (FDA 2891a) from FDA each year. Both are one-page, multicopy forms that are to be completed and sent to the FDA Device Registration and Listing Branch at the address given in the instructions for the form. If changes in registration status occur at other than the annual registration time, they must be submitted in a letter to FDA within 30 days after they occur. Under SMDA, distributors are now required to register with FDA.

Device Listing

Devices are to be listed on the "Device Listing Form" (FDA 2892). This is also a multicopy one-pager. After one form has been completed for each classified device marketed by the firm, the forms are returned to the FDA Device Registration and Listing Branch. Unlike registration, listing is not updated yearly.

Only when a significant change occurs in one or more of the data elements on the form, does the firm submit a new listing form containing the changes.

Premarket Notification [510(k)]

At least 90 days before it intends to market a device for the first time, a firm must submit to FDA's Document Mail Center a "Premarket Notification," also called a "510(k) submission." The 510(k) submission must contain sufficient information to show that a device is substantially equivalent to a predicate device, that is, a legally marketed device. A Premarket Notification also is required for a product that has been or is being marketed by a firm when there is a significant change or modification, including intended use of the device, that may significantly affect the safety or effectiveness of the device.

There is no form for 510(k) submissions; however, a format can be found in Section 807.87 of 21 CFR (Code of Federal Regulations). Each submission must contain:

- The name of the device (both trade, common or usual *and* classification name).
- The establishment registration number. If the firm is not yet registered, a statement to this effect is sufficient.
- The class of the device (if known), or a statement that the class is not known, indicating the appropriate panel.
- Action taken to conform to any applicable FDA Special Controls for a Class II device, if a special control has been issued.
- Proposed labels and labeling for the device, including any advertisements sufficient to describe the intended use of the product. Proposed labeling is sufficient.
- Persons submitting a premarket notification [510(k)] submission must provide to the FDA, as part of the submission, either an adequate summary of any information known about the device's safety and effectiveness or a statement that such information will be made available upon request by any person.
- Persons submitting a 510(k) for a class III device must include a certification that they have conducted a reasonable search of all information known or otherwise available to the manufacturer respecting the device (and others like it) and a summary of and citation to all adverse safety and effectiveness data respecting the device (and others like it).
- A statement (with accompanying data) indicating how the device is similar to and/or different from other comparable products that are already in commercial distribution.
- For a submission made because the device has undergone a change or modification that could significantly affect safety and effectiveness, sufficient data to show that consideration has been given to this change and its effect on the safety and effectiveness of the device.
- Any additional information requested by FDA to determine if the device is substantially equivalent. Such added information must be submitted within 30 days, or an extension of time to respond must be requested.

Good Manufacturing Practices

The Good Manufacturing Practices (GMP) regulation covers the methods, facilities, and controls used in pre-production design validation, manufacturing, packaging, storing, and installing medical devices. The GMP regulation identifies the essential elements required of the quality assurance program. FDA monitors compliance with the GMP regulation during inspection of the firm's manufacturing facilities.

To address the variety and complexity of devices, the GMP regulation designates two device categories: "noncritical" and "critical." General requirements apply to all devices, but critical devices must meet additional GMP requirements. A list of "Critical Devices" is available from the Division of Small Manufacturers Assistance.

INVESTIGATIONAL DEVICE EXEMPTION

To allow manufacturers of devices intended solely for investigational use to ship these devices for use on human subjects, the FD&C Act authorizes FDA to exempt these firms from certain requirements. This exemption is known as an Investigational Device Exemption (IDE) and applies only to investigational studies gathering safety and effectiveness data for a medical device when using human subjects. If a device is considered to present "significant risk," IDE applicants must submit information to FDA demonstrating that testing will be supervised by an Institutional Review Board (IRB), that appropriate informed consent will be obtained, and that certain records and reports will be maintained. For a "nonsignificant" risk device, submission to FDA is not necessary but IRB approval is still required.

A "significant risk" investigational device is one that:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is purported or represented to be for use in supporting or sustaining human life, and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease (or otherwise preventing impairment of human health) and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

Certain types of devices are exempted from the IDE regulation. These include custom devices, certain in vitro diagnostic devices, devices solely for veterinary use, and devices that are substantially equivalent to preamendment devices used for the same intended purpose. Preamendment devices are those commercially marketed before May 28, 1976.

PREMARKET APPROVAL

An approved Premarket Approval (PMA) application is somewhat like a "private license" granted to the applicant to market a particular medical device. Other firms seeking to market the same type of device for the same use must also have an approved PMA. Class III devices may require PMA application approval, Premarket Notification, or both.

Premarket approval requirements differ between "preamendment" and "postamendment" devices.

Preamendment devices are those in commercial distribution before May 28, 1976. FDA must use a regulatory process to call for PMAs for preamendment devices. The agency is calling for such PMAs, as required in the 1990 Safe Medical Devices Act.

Before requiring a firm to have an approved PMA application in order to continue marketing a preamendment medical device, FDA must wait 30 months from the effective date of a **final** classification regulation for the device or 90 days after publication of a final regulation requiring the submission of a PMA -- whichever is later.

Postamendment devices are those first commercially distributed after May 28, 1976. Manufacturers of Class III **postamendment** devices that are not substantially equivalent to **preamendment** Class III devices are required to obtain PMA application approval before marketing their device.

If a firm plans to market a device that is similar to a **preamendment** Class III device for which a PMA has **not** been called, a Premarket Notification should be submitted. If FDA finds the new device substantially equivalent to the preamendment device, it will then be subject to the same requirements as the preamendment device. If the device is not substantially

equivalent to the preamendment Class III device, then by statute a PMA is required *or* a firm may choose to petition to reclassify the device into Class I or Class II. SMDA provides for limited situations when information used in previous four-of-a-kind approved PMAs may be used by FDA in reviewing new Class III devices. Also, approved PMAs may be suspended temporarily.

SAFE MEDICAL DEVICES ACT

A number of requirements for devices are included in provisions of the Safe Medical Devices Act of 1990. Some of these provisions became effective immediately; others had later dates or require implementing legislation. SMDA requirements are extensive and the reader is encouraged to contact FDA for more specific information. Key SMDA highlights are:

- **Medical Device Reports**

  Manufacturers and Distributors. Manufacturers and distributors must submit Medical Device Reports (MDRs). They make such reports when they receive or otherwise become aware of information that reasonably suggests that a device they manufacture or distribute:

  (1) caused or contributed to a death, serious illness or serious injury; or

  (2) malfunctioned, and there is a probability that if the malfunction were to recur, the devices would cause or contribute to a death, serious injury or serious illness.

  User Facilities. Medical device user facilities (hospitals, nursing homes, ambulatory surgical facilities, and outpatient treatment and diagnostic facilities) are required to report incidents that reasonably suggest there is a probability that a medical device has caused or contributed to the death of a patient, or serious injury or serious illness of a patient.

  Certification. Manufacturers, importers, distributors and user facilities have to certify to FDA the number of reports they have submitted.

- **Tracking Requirements.** Manufacturers must have in place a method for tracking devices, the failure of which would be reasonably likely to have serious, adverse health consequences and which are:
  - a permanently implantable device, or
  - a life-sustaining or life-supporting device used outside a device user facility.

  FDA designates which devices require tracking.

- **Removals and Corrections.** Manufacturers, importers and distributors are required to report to FDA certain removals or corrections of a device.

- **Postmarket Surveillance.** Manufacturers are required to conduct postmarket surveillance, such as studies to gather data on the safety and effectiveness of a device, for certain devices introduced into interstate commerce after January 1, 1991. FDA designates which devices require postmarket surveillance.

- **Civil Penalties.** A manufacturer may be liable for a maximum civil penalty of $15,000 per violation of the FD&C Act, and a maximum of $1,000,000 per proceeding before an Administrative Law Judge.

- **FDA Recall Authority.** FDA now may require a recall of a medical device.

- **Good Manufacturing Practices.** The GMP now includes design validation requirements.

- **Other Changes.** These affect premarket notifications [510(k)s], premarket approvals (including those for preamendment Class III devices and transitional devices), and the classification process.

For additional information, contact the Division of Small Manufacturers Assistance at (800) 638-2041. From outside the United States, call (301) 443-6597. You may also FAX (301) 443-8818 or write to:

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